

### **REMARKS**

This paper is in response to the official action dated December 30, 2008, and the interview summary dated May 7, 2009, and a subsequent teleconference between the examiner and the undersigned on May 19, 2009. This paper is timely filed as it is accompanied by a petition for extension of time and authorization to charge our credit card account in the amount of the requisite fee. The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed, or which should have been filed herewith, to our Deposit Account No. 13-2855, under Order No. 29473/11899A.

Claims 1 and 4-12 are pending, but claim 5 has been withdrawn from consideration.

Claims 1, 4, and 6-12 remain rejected under 35 U.S.C. §112, first paragraph, as assertedly failing to comply with the written description requirement. Claims 1, 4, and 6-12 also remain rejected under 35 U.S.C. §103(a) as assertedly unpatentable over Mühlrad et al., *J. Exp. Med.*, 185:1951-1958 (1997) ("Mühlrad") in view of international patent publication no. WO 98/27110 and U.S. Patent 4,916,118 to Fidler et al. ("Fidler"). Claims 1, 4, and 6-12 also remain provisionally rejected for obviousness-type double patenting over claims 1-3, 6-8, 10, and 11 of copending patent application serial no. 10/509,917 in view of Mühlrad. Finally, claims 1, 4, and 6-12 remain rejected under 35 U.S.C. §112, second paragraph, as assertedly indefinite.

The various bases for the claim rejections have been addressed previously, and applicants' prior remarks concerning same are reproduced herein for the examiner's convenience.

Additionally, in response to the examiner's request (which was articulated during the May 19, 2009, teleconference referenced above), the applicants also explain herein (1) the claims are entitled to the international application (PCT) filing date of May 19, 1999, and (2) the facts demonstrating their possession of both R- and S- enantiomers.

### **SUMMARY**

The present application (U.S. serial no. 10/748,033) is a continuation of U.S. application serial no. 09/716,778, which is a continuation-in-part of international application no. PCT/EP99/03436. The present application claims are directed to the

R-enantiomer of lipopeptide MALP-2. U.S. application serial no. 09/716,778 (now abandoned) included claims directed to the S-enantiomer, whereas international application no. PCT/EP99/03436 included claims directed to the R-enantiomer. The differences in the enantiomer claimed resulted from an incorrect attribution of the configuration of the tested compounds.

During the May 19, 2009, teleconference, the applicants respectfully submitted that the pending claims are entitled to the international filing date, and that any mistake made in claiming the invention in the parent CIP was merely one of attribution – not possession, i.e., the same compound gave superior results no matter what it was called. Furthermore, the applicants pointed out that both enantiomers were tested and thus the inventors had possession of both compounds at the time of filing all involved applications.

In response, the examiner requested a showing that the continuity chain has been perfected (i.e., that U.S. application no. 10/748,033 is formally entitled to the international filing date) and the inventors had possession of both R- and S-enantiomers at the time of filing all involved applications. The requested showing follows.

### **PERFECTION OF CONTINUITY CHAIN**

The present application (U.S. application serial no. 10/748,033) was filed on December 30, 2003, and is a continuation of U.S. application serial no. 09/716,778, filed on November 20, 2000, which is a continuation-in-part of international application no. PCT/EP99/03436, filed on **May 19, 1999**. U.S. application serial no. 10/748,033 also claims the priority benefit under 35 USC 119 of German application 198 22 820.1, filed on **May 20, 1998**.

The patent application transmittal and preliminary amendment filed in the present application establish continuity between the present application, U.S. application serial no. 09/716,778, and international application no. PCT/EP99/03436. The Declaration for Patent Application and Power of Attorney and Supplemental Declaration filed in this application (and in U.S. application serial no. 09/716,778) also indicate that U.S. application serial no. 09/716,778 claims priority to international application no. PCT/EP99/03436 and German application 198 22 820.1.

The filing receipt mailed February 2, 2005 confirms the priority claims. In addition, the PTO acknowledged receipt of certified copies of all the priority documents for the present application in office actions mailed September 14, 2006, September 7, 2007, and December 30, 2008.

In view of the foregoing, the applicants respectfully submit that the continuity chain has been perfected and that the international (PCT) filing date is applicants' earliest effective U.S. filing date.

### **POSSESSION OF BOTH ENANTIOMERS**

The applicants respectfully submit that the pending claims are entitled to the international (PCT) filing date of May 19, 1999.

In support, the applicants direct the examiner to results from experimental testing comparing the activities of both the R- and S-enantiomers of MALP-2 and the racemic mixture, which are included in international application no. PCT/EP99/03436 and U.S. application serial nos. 09/716,778 and 10/748,033. In view of the foregoing, the applicants had possession of both enantiomers and the racemate throughout the domestic priority chain and are entitled to the earliest domestic filing date of the PCT application.

### **In Vivo Effect of R-MALP-2 and S-MALP-2 Following Intraperitoneal Injection (Example 3 in PCT/EP99/03436, U.S. 09/716,778, and U.S. 10/748,033)**

To assess the importance of the asymmetric carbon atom at position C2 of the dihydroxypropyl group in the in vivo activity of the lipopeptides, S-MALP-2 or R-MALP-2 is injected intraperitoneally into mice. The composition of the peritoneal leukocyte population is determined 3 days following injection. The results, summarized in Table 2 of each of the involved applications, indicate one enantiomer is clearly more effective than the other configuration. Clearly, the identity of the more effective enantiomer did not change between the time the PCT and U.S. applications were filed. Rather, a mistake in attribution was made, which was subsequently corrected in the claims of the present application (as explained in further detail below, and in the attached declaration of (inventor) Dr. Peter F. Mührladt). The results demonstrating significantly increased leukocyte inflow are correctly attributed

to R-MALP-2 in PCT/EP99/03436 and incorrectly assigned to S-MALP-2 in U.S. 09/716,778.<sup>1</sup>

**In Vivo Effect of Racemic MALP-2 Following Intraperitoneal Injection  
(Example 2 in U.S. 09/716,778, and U.S. 10/748,033; Example 1 in  
PCT/EP99/03436)**

To assess the in vivo effect of both enantiomers combined, racemic MALP-2, free or incorporated into liposomes, is injected into the peritoneal cavity of mice, and the inflow of granulocytes and macrophages following injection is measured for up to 72 hours. Both the free and liposomal MALP-2 caused significant increases in peritoneal leukocytes and granulocytes 24 hours after injection (Figures 2 and 3 in U.S. application serial nos. 09/716,778 and 10/748,033; Figures 1 and 2 in PCT/EP99/03436).

In view of presence of applicants' experiments detailing testing of R- and S-enantiomers of MALP-2 and the racemic mixture in each of PCT/EP99/03436 and U.S. application serial nos. 09/716,778 and 10/748,033, the applicants respectfully submit that continuity has been maintained and that they had possession of both enantiomers and the racemate at least as early as the earliest effective U.S. filing date (notwithstanding the misattribution of results in U.S. 09/716,778).

**CLAIM REJECTIONS – 35 U.S.C. §112, 1<sup>ST</sup> PARAGRAPH**

Claims 1, 4, and 6-12 have been rejected under 35 U.S.C. §112, first paragraph, as assertedly failing to comply with the written description requirement. The applicants respectfully traverse the rejections.

As previously submitted, the applicants mistakenly attributed their experimental results for lipopeptides or lipoproteins having the "R" configuration to lipopeptides or lipoproteins having the "S" configuration and vice versa in this patent application. However, the stereochemistry of the lipopeptides or lipoproteins is described correctly in the priority application for this application (i.e., international application no. PCT/EP99/03436). In support of this statement, the examiner's attention is directed to claim 1 of PCT/EP99/03436, which claims the "absolute R-Konfiguration" and to page 1 of the attached declaration of (inventor) Dr. Peter F.

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<sup>1</sup> The present application description has not been amended yet to clarify the correct attribution of results, but the claims have been amended to recite the desired stereochemistry.

Mühlradt. At page 1 of the attached declaration, inventor Mühlradt explains that “PCT/EP 99/03 436 characterizes the utilized lipopeptides and lipoproteins by their R-configuration which is in accordance with my understanding on the filing day....”

At the paragraph bridging pages 1 and 2 of the attached declaration, inventor Mühlradt further describes that subsequent to the filing date of PCT/EP99/03436, he learned of Metzger *et al.*, *J. Medicinal Chem.*, 34:1969-1974 (1991), and that this document mistakenly led him to believe the correct configuration of the utilized lipopeptides or lipoproteins (i.e., those lipopeptides or lipoproteins showing increased activity relative to their enantiomer) was the S-configuration. Consequently, the U.S. application serial no. 09/716,779, which is continuation-in-part of PCT/EP99/03436, was “amended” to characterize the utilized lipopeptides or lipoproteins by an S-configuration. At page 2 of the declaration, inventor Mühlradt further describes that he came to understand that the original international application described the correct configuration and that the reliance on Metzger *et al.* was misplaced. Paragraph [0038] of U.S. Patent Publication No. 2004/0127405 to Mühlradt *et al.*, which describes the consequences of applicants’ reliance on Metzger *et al.*, *J. Medicinal Chem.*, 34:1969-1974 (1991), is wholly consistent with applicants’ previous statements.

Furthermore, the applicants respectfully submit that the instant specification demonstrates their possession of methods of treating a wound in an animal comprising administering lipopeptides or lipoproteins in accordance with the structure shown in claim 1, whether the lipopeptide or lipoprotein has the absolute R configuration, as recited in claim 1, the absolute S configuration, or an enantiomeric mixture thereof. In this regard, the applicants again respectfully direct the examiner’s attention to example 3, which demonstrates their possession of methods of treating animals with different enantiomers of the same lipopeptide. While the results are mistakenly attributed in the present U.S. application, the inventors’ possession of methods using lipopeptides or lipoproteins having both the R and S configurations (as of the earliest effective and continuation-in-part filing dates) cannot be questioned in view thereof.

It is respectfully submitted that the inventors’ possession of the claimed subject matter as of the priority application filing date has been established. Accordingly, the written description rejections of claims 1, 4, and 6-12 should be removed.

**CLAIM REJECTIONS – 35 U.S.C. §103**

Claims 1, 4, and 6-12 remain rejected under 35 U.S.C. §103(a) as obvious over Mühlradt in view of WO 98/27110 and Fidler. The applicants respectfully traverse the obviousness rejections for the reasons provided in the response dated February 14, 2007 (received by the office on February 20, 2007). Removal of these rejections is respectfully requested in view thereof.

**CLAIM REJECTIONS – DOUBLE PATENTING**

The applicants will address these provisional rejections if and when they should become mature.

**CLAIM REJECTIONS – 35 U.S.C. §112, 2<sup>ND</sup> PARAGRAPH**

Claims 1, 4, and 6-12 remain rejected as assertedly indefinite. The applicants respectfully traverse the obviousness rejections for the reasons provided in the response electronically filed with the Patent Office in January 7, 2008. Removal of these rejections is respectfully requested in view thereof.

**CONCLUSION**

It is submitted that the application is in condition for allowance. Should the examiner wish to discuss any matter of form or procedure in an effort to advance this application to allowance, he is respectfully invited to telephone the undersigned attorney at the indicated telephone number.

Respectfully submitted,

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